

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

Claims 1-44 (Canceled).

45. (Currently amended) A method of cleaving a nucleic acid target in a mammalian cell in vitro comprising contacting the cell with a single-stranded siRNA molecule, wherein the single-stranded siRNA molecule:
is complementary to the nucleic acid target molecule;
is from 14 to 50 nucleotides in length; and
comprises a phosphate analog at the 5'-terminus; and
thereby cleaving the nucleic acid target molecule in the cell.

46. (Previously presented) The method of claim 45 wherein the single-stranded RNA molecule is from 15 to 29 nucleotides in length.

47. (Previously presented) The method of claim 45 wherein at least the 14 5'-terminal nucleotides of the single-stranded RNA molecule are complementary to the nucleic acid target molecule.

48. (Previously presented) The method of claim 45, wherein the phosphate analog at the 5'-terminus of the single-stranded RNA molecule is selected from among: a 5'-guanosine cap, a 5'-adenosine cap, a 5'-monothiophosphate, a 5'-monodithiophosphate, a 5'-phosphorothiolate, a 5'-phosphoramidate, a 5'-alkylphosphonate, and a 5'-alkyletherphosphonate.

49. (Previously presented) The method of claim 45, wherein the phosphate analog at the 5'-terminus of the single-stranded RNA molecule is selected from among: a 5'-monophosphate, a 5'-diphosphate, and a 5'-triphosphate.

50. (Previously presented) The method of claim 49, wherein the phosphate analog at the 5'-terminus of the single-stranded RNA molecule is a 5'-triphosphate.

51. (Previously presented) The method of claim 45, wherein the phosphate analog at the 5'-terminus of the single-stranded RNA molecule comprises a monophosphate, a diphosphate, or a triphosphate in which at least one oxygen atom of the monophosphate, diphosphate, or triphosphate has been replaced with a sulfur atom.

52. (Previously presented) The method of claim 51, wherein the phosphate analog is selected from among 5'-alpha-thiotriphosphate and 5'-gamma-thiotriphosphate.

53. (Previously presented) The method of claim 45, wherein the phosphate analog at the 5'-terminus of the single-stranded RNA molecule is an alkylphosphonate.

54. (Previously presented) The method of claim 53, wherein the alkylphosphonate has the formula: $RP(OH)(O)-O-5'$ or $(OH)_2(O)P-5'-CH_2-$, where R is a C_1-C_3 alkyl.

55. (Previously presented) The method of claim 45, wherein the phosphate analog at the 5'-terminus of the single-stranded RNA molecule is an alkyletherphosphonate.

56. (Previously presented) The method of claim 55, wherein the alkyletherphosphonate has the formula: $RP(OH)(O)-O-5'$, where R is an alkylether.

57. (Currently amended) The method of claim 45, wherein the single-stranded RNA molecule comprises at least one sugar or backbone modified nucleoside at the 3' terminus, wherein at least the 15 nucleotides at the 5' terminus are unmodified.

58. (Currently amended) The method of claim 57, wherein at least one modified nucleoside comprises a sugar modification wherein the 2'OH group is replaced by a group selected from the group consisting of H, OR, R, halo, SH, SR,

NH₂, NHR, NR₂, and CN, wherein R is selected from the group consisting of C₁-C₆ alkyl, alkenyl, alkynyl, and methoxyethoxy.

59. (Currently amended) The method of claim ~~58, wherein at least one~~ sugar modification is a 2'-sugar modification ~~57, wherein in said backbone modified~~ nucleoside a phosphoester group connecting adjacent ribonucleotides is replaced by a modified group selected from the group consisting of a phosphorothioate, a phosphorodithioate, a N3'-O5' phosphoramidate group and a N5'-O3' phosphoramidate group.

60. (Previously presented) The method of claim 45, wherein the single-stranded RNA molecule comprises at least one phosphorothioate linkage.

61. (Currently amended) The method of claim 45, wherein the single-stranded RNA molecule comprises at least one mismatch at the 3' terminus, wherein at least the 15 nucleotides at the 5' terminus are completely complementary to the nucleic acid target molecule.

62. (Previously presented) The method of claim 45, wherein the single-stranded RNA molecule comprises a region at the 3'-terminus comprising at least one adenosine, guanosine or combination thereof.

63. (Previously presented) The method of claim 45, wherein the cell is a eukaryotic cell.

64. (Previously presented) The method of claim 63, wherein the eukaryotic cell is a plant cell.

65. (Previously presented) The method of claim 63, wherein the eukaryotic cell is an animal cell.

66. (Previously presented) The method of claim 65, wherein the animal cell is selected from the group consisting of a mammalian cell, an embryonic cell, a pluripotent stem cell, a tumor cell and a virus-infected cell.

67. (Previously presented) The method of claim 66, wherein the tumor cell is a teratocarcinoma cell.

68. (Previously presented) The method of claim 65, wherein the animal cell is a human cell.

69. (Currently amended) A method of activating RISC and thereby cleaving a nucleic acid target molecule in a mammalian cell in vitro comprising contacting the cell with a single-stranded oligonucleotide, wherein the single-stranded oligonucleotide:

is complementary to the nucleic acid target molecule;
is from 15 to 29 nucleotides in length; and
comprises a phosphate analog at the 5'-terminus; and
thereby activating RISC and cleaving the nucleic acid target molecule in the cell.

70. (Previously presented) The method of claim 69 wherein at least the 14 5'-terminal nucleotides of the single-stranded oligonucleotide are complementary to the nucleic acid target molecule.

71. (Previously presented) The method of claim 69, wherein the phosphate analog at the 5'-terminus of the single-stranded oligonucleotide is selected from among: a 5'-guanosine cap, a 5'-adenosine cap, a 5'-monothiophosphate, a 5'-monodithiophosphate, a 5'-phosphorothiolate, a 5'-phosphoramidate, a 5'-alkylphosphonate, and a 5'-alkyletherphosphonate.

72. (Previously presented) The method of claim 69, wherein the phosphate analog at the 5'-terminus of the single-stranded oligonucleotide is selected from among: a 5'-monophosphate, a 5'-diphosphate, and a 5'-triphosphate.

73. (Previously presented) The method of claim 72, wherein the phosphate analog at the 5'-terminus of the single-stranded oligonucleotide is a 5'-triphosphate.

74. (Previously presented) The method of claim 69, wherein the phosphate analog at the 5'-terminus of the single-stranded oligonucleotide comprises a monophosphate, a diphosphate, or a triphosphate in which at least one oxygen atom of the monophosphate, diphosphate, or triphosphate has been replaced with a sulfur atom.

75. (Previously presented) The method of claim 74, wherein the phosphate analog is selected from among 5'-alpha-thiotriphosphate and 5'-gamma-thiotriphosphate.

76. (Previously presented) The method of claim 69, wherein the phosphate analog at the 5'-terminus of the single-stranded RNA molecule is an alkylphosphonate.

77. (Previously presented) The method of claim 76, wherein the alkylphosphonate has the formula: $RP(OH)(O)-O-5'$ or $(OH)_2(O)P-5'-CH_2-$, where R is a C_1-C_3 alkyl.

78. (Previously presented) The method of claim 69, wherein the phosphate analog at the 5'-terminus of the single-stranded RNA molecule is an alkyletherphosphonate.

79. (Previously presented) The method of claim 78, wherein the alkyletherphosphonate has the formula: $RP(OH)(O)-O-5'$, where R is an alkylether.

80. (Currently amended) The method of claim 69, wherein the single-stranded oligonucleotide comprises at least one sugar or backbone modified nucleoside at the 3' terminus, wherein at least the 15 nucleotides at the 5' terminus are unmodified.

81. (Currently amended) The method of claim 80, wherein at least one modified nucleoside comprises a sugar modification wherein the 2'OH group is replaced by a group selected from the group consisting of H, OR, R, halo, SH, SR, NH_2 , NHR, NR_2 , and CN, wherein R is selected from the group consisting of C_1-C_6 alkyl, alkenyl, alkynyl, and methoxyethoxy.

82. (Currently amended) The method of claim 81, ~~wherein at least one sugar modification is a 2'-sugar modification~~ 80, wherein in said backbone modified nucleoside a phosphoester group connecting adjacent ribonucleotides is replaced by a modified group selected from the group consisting of a phosphorothioate, a phosphorodithioate, a N3'-O5' phosphoramidate group and a N5'-O3' phosphoramidate group.

83. (Previously presented) The method of claim 69, wherein the single-stranded RNA molecule comprises at least one phosphorothioate linkage.

84. (Currently amended) The method of claim 69, wherein the single-stranded RNA molecule comprises at least one mismatch at the 3' terminus, wherein at least the 15 nucleotides at the 5' terminus are completely complementary to the nucleic acid target molecule.

85. (Previously presented) The method of claim 69, wherein the single-stranded RNA molecule comprises a region at the 3'-terminus comprising at least one adenosine, guanosine or combination thereof.

86. (Previously presented) The method of claim 69, wherein the cell is a eukaryotic cell.

87. (Previously presented) The method of claim 86, wherein the eukaryotic cell is a plant cell.

88. (Previously presented) The method of claim 86, wherein the eukaryotic cell is an animal cell.

89. (Previously presented) The method of claim 88, wherein the animal cell is selected from the group consisting of a mammalian cell, an embryonic cell, a pluripotent stem cell, a tumor cell and a virus-infected cell.

90. (Previously presented) The method of claim 89, wherein the tumor cell is a teratocarcinoma cell.

91. (Previously presented) The method of claim 89, wherein the animal cell is a human cell.

92. (Previously presented) The method of claim 45, wherein the single-stranded siRNA molecule is a single-stranded antisense siRNA molecule.